Author's response to reviews

Title: Association between occupational exposure and the clinical characteristics of COPD

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Author's response to reviews: see over
Dear Editor

Here you will find the revised version of our manuscript entitled “Association Between Occupational Exposure And The Clinical Characteristics Of COPD”. Below are the detailed point-by-point answers to the reviewers’ comments.

**Reviewer 1**

The few changes I suggested have been adequately addressed. I note the comments and response to the other reviewers. I believe that the manuscript has benefitted greatly from the review process and it is better and more robust with the changes made. It is clear that the other reviewers (and authors) have contributed a significant amount of time and effort to make this a good manuscript. The messages drawn from the work is now more clearly made and the strengths and weaknesses of the work better described.

We thank the reviewer for these comments.

**Reviewer 2**

I am satisfied with your responses to my previous comments, with one exception; I still do not understand why you cannot carry out multiple regression analysis. I can see that the logistic model may be difficult to handle, but why not use a multiple linear model instead, such as FEV1=age smoking VGDF atopy. The reason for me to be persistent about this is that such a model gives a much more informative adjustments for confounding. If you choose to not perform multiple regression analysis, please then motivate that in the manuscript.

The multivariate analysis suggested by the reviewer aims at assessing the respective “weight” of various risk factors of COPD, as determinants of the severity of airflow obstruction, as assessed by FEV1. This analysis was indeed performed in an exploratory perspective, using two models: one was a logistic regression analysis with GOLD stage as dependent variable, the other was a multilinear regression with FEV1 (%) predicted as the dependent variable. Smoking was accounted for using cumulative consumption in pack-years and smoking status at inclusion (present vs past smoking). Variables reflecting atopy were patient-reported hay fever and familial history of atopy. With the first model, only less than 2% ($R^2=0.018$, p value of the model: 0.46) of variations in the GOLD classification could be explained by risk factors. In the second model, $R^2$ was even lower (0.0089, with a p value for the model of 0.28). Thus, it can be concluded that, in this population of smokers and ex-smokers, risk factors (age, smoking, occupational exposure, atopy) are very poorly correlated with the severity of airflow obstruction, which makes it impossible to draw any conclusion as to their
respective weight. Since this was not the research question we were addressing in the manuscript, we did not add these results to the manuscript. However, if the editor wishes, we could add a short paragraph in the discussion section.

Quality of written English:

Needs some language corrections before being published

The manuscript has been reviewed by a native English-speaking physician.

Reviewer 3

I have looked at the revised manuscript and the authors have as much as possible responded to my comments. I made some suggestions to their manuscript, see link.

We thank you for your suggestions and have changed the manuscript as requested.

Reviewer 4

Major Compulsory Revisions

1. The authors have addressed the major compulsory revision
   They have changed the title from Impact of occupational exposure on COPD to Impact of occupational exposure on the clinical characteristics of COPD which is in agreement with suggestion.

Minor essential revision
2. The abbreviation BPCO was well addressed by the authors but other ones were left out.
   GOLD : p 6, the abbreviation has been expanded in the text: Methods, population.
   AHR : p 12: It is used for the first time in the paragraph
   “association between occupational exposure, asthma-like symptoms and lung function” and the full name: “airway hyperresponsiveness” is written just before the abbreviation.
   SGRQ, This abbreviation has been expanded in the Methods section, paragraph “data collection”, p 7
   SAS : This is the name of the software.
   were left out.

3. The objectives of the study in the last paragraph on page 4 has been re written and phrased into a single sentence
4. The authors reply and explanation on the hospital anxiety and depression scale is well accepted. I totally agree with the withdrawal from the manuscript in view of the missing data.
5. There few typographical error and spelling mistakes have corrected
6. With reference to the statistical analysis, the author should clearly provide reasoning(s) why median was used and not mean or mode. The authors need to be aware that this article if published may be reviewed by residents during their journal club or read by someone with an inadequate statistical background.

Since some variables were not continuously distributed, non-parametric tests were performed for comparisons and median values and interquartile ranges were used to describe the whole set of variables.

This point has been added to the Statistics paragraph of the Methods section.

7. Other suggested corrections have been effected.

8. The authors need to include a citation(s) for this statement:

Patients were categorized
(i) as current smokers or, past exsmokers (smoking cessation at least 12 months ago), or never smokers,and
(ii) as smokers or ex-smokers of # or < 20 pack-years

As requested, a reference was added in the text.

Reviewer 5

The authors have satisfactorily replied to the comments.